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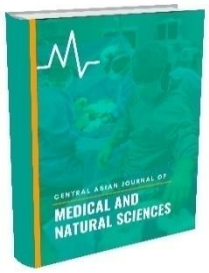

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The State of Changes in the Immune System in Patients Chronic Obstructive Lung Disease in Survivors of Covid-19

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Annotation: Questions related to the topic of the joint course of the new coronavirus infection COVID-19 and chronic obstructive pulmonary disease (COPD) are currently very relevant. This is due to the similarity of clinical manifestations, the complexity of diagnosis. COPD patients with comorbid diseases infected with SARS-CoV-2 represent a particularly vulnerable group of people with a complicated course and often an unfavorable outcome of the disease. In light of the above, the study of laboratory indicatorsfeatures of the course and risk factors for cardiovascular complications, the development of effective methods for the treatment and rehabilitation of patients with COPD in combination with the metabolic syndrome against the background of COVID-19 remains an urgent problem. A new effective approach has been developed for the early diagnosis of chronic obstructive pulmonary disease (COPD) based on the clinical and immunological characteristics of the disease. The study included 46 patients with COPD who were in the departments of allergology and pulmonology of the Samarkand city medical association in 2022-2023. Changes in the profile of interleukins in blood serum depending on the stage and sex in COPD are described in detail.

Key words: chronic obstructive pulmonary disease, coronovirus infection, enzyme immunoassay, in those who have had COVID-19, interleukin.

Inroduction. After the pandemic COPD in COVID-19 survivors, being a widespread disease among the world's population, causes serious socio-medical and economic harm and leads to disability. According to epidemiological studies, the prevalence of COPD in the world averages from 10% to 47%. (1,4,8,11). In Russia, according to scientific research, more than 25% of patient visits to the doctor are respiratory diseases (2,6,10). In recent years, the incidence of chronic lung pathology has been growing all over the world, including in Uzbekistan, which is characterized by an increase of 21% in relation to general diseases. (3,5,7). Currently, many risk factors are known that contribute to the development of COPD, but the most common among them are smoking and infectious factors,

which accompany 50-60% of cases. COPD is the most common respiratory disease and it is believed that infection contributes to the development of immune disorders and causes relapses. Therefore, determining the etiology of COPD, predicting its course and searching for new treatment methods is an important task in clinical pulmonology (9,12,13).

A number of scientific studies are being conducted around the world aimed at achieving high effectiveness in improving the early diagnosis, treatment and prevention of COPD. At the same time, one of the important tasks in COPD in survivors of COVID-19 is to determine the role of coronavirus infection in the pathogenesis of the disease to determine the severity, early diagnosis and prognosis of the disease.

Objective: to study an effective approach to early diagnosis of COPD in COVID-19 survivors based on the clinical and immunological characteristics of the disease.

Materials and methods: the study included 46 patients with COPD who had COVID-19 and were in the allergy and pulmonology departments of the Samarkand City Medical Association in 2022-23. When making a diagnosis, the patients' complaints, medical history, heredity, and course of the disease were taken into account. All patients were diagnosed with broncho-obstructive syndrome with a negative reaction to the bronchodilator test. Bronchial patency was assessed by forced expiratory volume in 1 second (FEV1) and forced vital capacity (FVC), the FEV1/FVC index. The indicators FEV1 < 80% and FEV1/FVC < 70% were taken as bronchial obstruction.

Results. All statistical processing of the obtained results was carried out using the software package “Statistic for Windows 7.0” (Stat Soft), Microsoft Excel 2007 software using parametric and nonparametric analysis methods. The results of sample studies using parametric methods are presented as M (mean value) ± m (standard error). The reliability of the results obtained was assessed using the Student's test (t) for dependent and independent samples; the difference was considered statistically significant at $p < 0.05$.

Discussion. There was an increase in the parameters of pro-inflammatory cytokines in patients with COPD who had suffered COVID-19, in particular, IL-1b was significantly increased 60.8 ± 0.4 pg/ml, compared with the control group 35.9 ± 0.3 pg/ml . ($r < 0.02$). A study of the concentrations of the IL-1b product showed that the amount of pro-inflammatory cytokines in the peripheral blood was high regardless of the period of the disease, which is confirmed by the following indicators during exacerbation - 69.5 ± 0.04 pg/ml and in remission - 49.6 ± 0 .08 pg/ml.

Studies have shown that the study of immunological mechanisms in the pathogenesis of COPD in survivors of COVID-19 plays an important role in the development and continuation of the inflammatory process in the respiratory tract.

When distributing patients by gender, the following levels of serum IL-1b were recorded in men: 75.9 ± 0.3 pg/ml and in women 58.50 ± 0.4 pg/ml $p < 0.02$. It is obvious that interleukin IL-1b, increasing more often in men, causes a higher degree of development of the inflammatory process in this sex in our studies.

The next stage of our study was to study the pro-inflammatory cytokine IL-8 in the peripheral serum of patients with COPD who had recovered from COVID-19. We found a significant increase in IL-8 to 86.2 ± 5.0 pg/ml, and in the control group this figure was 28.9 ± 3.31 pg/ml. ($r < 0.01$).

A study of IL-8 concentrations showed that the amount of pro-inflammatory cytokines in peripheral blood was also high, regardless of the period of the disease. Consequently, the concentration of IL-8 cytokines in patients was 53.5 ± 2.14 pg/ml during exacerbation and 40.6 ± 1.18 pg/ml during remission, respectively. Data obtained from the study of immunological mechanisms in pathogenesis COPD in survivors of COVID-19 may serve as a basis for recommending a new differentiated

approach to diagnosis and pathogenetic treatment.

Thus, the determination of interleukin-8 makes it possible to assess the presence of complex cross-links in different parts of the immune response in COPD and to correctly select immunotropic therapy.

Alveolar macrophages are known to bind microbes that carry secretory IgA. sIgA deficiency leads to a decrease in the phagocytic activity of macrophages. As a result, there is a violation of the clearance of the lumen of the bronchial mucosa, microbial colonization and chronic inflammation.

The next stage of the study was to study the cytokine status in bronchoalveolar lavage in patients COPD in survivors of COVID-19. When analyzing the parameters, it was found that in patients the level of IL-1b in BAL fluid was significantly increased and averaged (142.5 ± 3.31 pg/ml) compared to the control group (34.2 ± 2.14 pg/ml). (r <0.01). It was also found that these indicators, regardless of the stage of the disease, had high values: during exacerbation of the disease - 140.9 ± 1.18 pg/ml, in remission - 130.5 ± 1.08 pg/ml, respectively. Similar values were observed when analyzing the level of IL-8 in BAL on average - 556.9 ± 5.0 pg/ml, and in the control group - 44.2 ± 3.31 pg/ml (r <0.01). Depending on the stage of the disease, these indicators varied and were: in the acute stage - 501.9 ± 2.14 pg/ml, in remission - 409.5 ± 1.18 pg/ml.

The analysis showed that the amount of sIGA in BAL fluid was significantly reduced in COPD patients who had recovered from COVID-19. It should be noted that the level of sIgA in patients with COPD X after COVID-19 was reduced and averaged 7.3 ± 5.0 pg/ml, and in the control group 15.4 ± 3.31 pg/ml (r< 0.01). Depending on the stage of the disease, the indicators were as follows: during exacerbation - 5.3 ± 2.14 pg/ml and during remission - 6.2 ± 1.18 pg/ml, respectively.

Thus, taking into account the above, we can draw the following conclusion: changes in the concentration of proinflammatory cytokines have a direct relationship with the degree of development of the inflammatory process during COPD and can be used for diagnostic purposes. In COPD, microbial colonization increases as a result of immune system deficiency, leading to exacerbation of the disease (Figure 1).

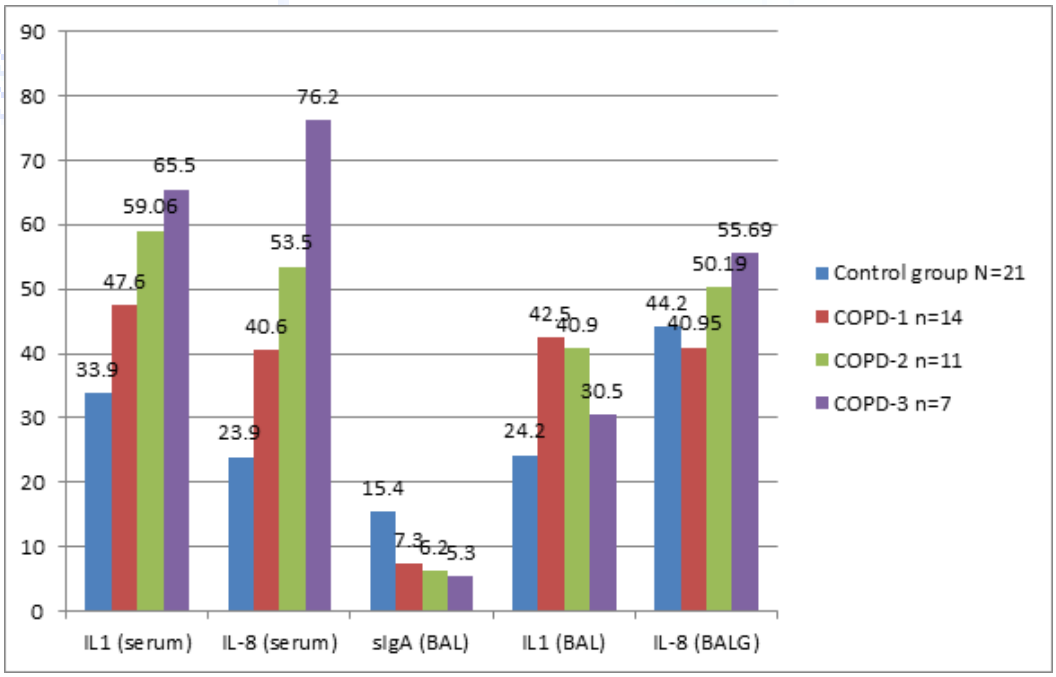

Figure 1. Differences in inflammatory biomarkers depending on the severity of the disease

Note - The differences are significant regarding the indicators of the control group *(t-4.6 p<0.01, p<0.02)

In conclusion, it is worth noting that the identified properties of sIgA, IL1b and IL-8 in the blood serum and bronchoalveolar fluid of patients with COPD in those who have had COVID-19 should be assessed as a correlation of complex relationships between different types of immune systems.

Conclusions:

1. In patients with COPD, there is an increase in the blood serum and bronchoalveolar lavage fluidIL-1β,IL-8,with a significant decrease in sIGA levels. This indicates the relationship between the general and local immune systems in the development of inflammation.

2. Thus, in patients with COPD in those who have had COVID-19. The content of both pro-inflammatory and anti-inflammatory cytokines depends on the severity of the disease. As a result of a study, in patients with COPD in those who have had COVID-19 in the phase of clinical remission, hypercytokinemia was recorded due to the high content of pro-inflammatory and anti-inflammatory cytokines at the systemic and local levels.

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